

REMARKS

Claims 1-4, 20-25, 28 and 30-31 have been cancelled, and Claims 13 and 29 amended to more definitely set forth the invention and obviate the rejections. This amendment is deemed not to add new matter. Claims 13-16, 26-27 and 29 remain in the application.

Reconsideration is respectfully requested of the rejection of claims 1-4, 13-16, 20, 25, 30 and 31 under 35 U.S.C. §103(a) as being unpatentable over N'guyen et al. (5,023,235) in view of Katsumata, et al. (5,601,806).

The principal N'Guyen, et al. reference discloses an antioxidant system comprised of at least one ascorbyl ester stabilized with at least one complexing agent (such as EDTA, the pentasodium salt of diethylenetriamine pentacetic acid, hexadecylamine salicylate (HDAS), citric acid, tartaric acid and its sodium salt, phytic acid, dibenzylidithiocarbamate, or mixtures thereof) and at least one thiol (such as N-acetyl cysteine, glutathione or a mixture thereof). The object of N'Guyen et al. is to inhibit oxidation of fatty bodies when same are "incorporated, for example, in food compositions or in cosmetics" (see column 1, lines 18-20).

N'Guyen, et al. recognized a synergistic effect based on the combination of the anti-oxidizing effects of tocopherols and

caffeic acid, and further state that the synergistic effect can be improved when the antioxidant system is based on a tocopherol in combination with a polypeptide (see column 2, lines 47-64). Importantly, however, as the Examiner has correctly acknowledged in the instant Office Action, there is no disclosure, teaching or suggestion whatsoever of including a metabolic intermediate of a sulphure containing amino acid (such as thiotaurine or hypotaurine) in the composition of N'Guyen, et al. to improve the synergistic effect, as now required in the claims as amended herein.

Furthermore, there is no teaching or suggestion of the link between environmental stress induced on the skin by contact with tobacco smoke, the accompanying increase in ultraweak chemiluminescence, and the method of suppression thereof. Rather, that teaching or suggestion comes only from the present invention, and constitutes an important element or aspect thereof.

The secondary Katsumata, et al. '806 reference is concerned with methods for scavenging (eliminating) active oxygen compounds and preventing damage from ultraviolet B rays (UVB) using taurine and its analogues, especially aminothiosulfonic acids. In particular, Katsumata, et al. are concerned with mimicking the function of superoxide dismutase (SOD), a naturally occurring substance in the body which decomposes and detoxifies superoxides caused by exposure of the skin to UVB radiation (see column 3,

last paragraph).

In particular, Katsumata, et al. disclose that thiotaurine, the main component of the cited reference, destroys superoxides, singlet oxygen and peroxide (see Experiments 1 and 4). Further, the oxidation of oil is disclosed. If, during such oxidation, thiotaurine is present, thiotaurine prevents oxidation of oil and amino acids. However, oxidation of such components is caused ALSO by free radicals, of which there is no mention or disclosure in the cited '806 reference.

Furthermore, in contrast to the disclosure of Katsumata, et al. concerning preventing oxidation of certain elements in the skin caused by exposure of the skin to UVB radiation, the present invention provides a *method of treating environmental stress due to exposure of the skin to tobacco smoke by suppressing ultraweak chemiluminescence caused by contact of the skin with tobacco smoke by applying the liniment claimed herein*. Such method, as claimed herein, is neither disclosed nor suggested by Katsumata, et al., and constitutes an important element or aspect of the present invention.

In order for a combination of references to render an invention obvious, it must be obvious that their teachings can be combined. *In re Avery* 518 F2d 1228, 186 USPQ 161 (CCPA 1975). Obviousness cannot be established by combining the teachings of

the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination. *In re Geiger* 815 F2d 686, 2 PQ2d 1276 (CAFC 1976). The references viewed by themselves, and not in retrospect, must suggest doing what applicant has done. *In re Schaffer* 229 F2d 476, 108 USPQ 326 (CCPA 1956); *In re Skoll* 523 F2d 1392, 187 USPQ 481 (CCPA 1975).

Importantly, Katsumata, et al. fail to teach or suggest combining thiotaurine and/or hypotaurine with ascorbic acid, citric acid and/or glutathione (the composition of N'Guyen) to obtain a synergistic effect, as contemplated by the Examiner. Further, there is believed to be no foundation for finding that there would have been an expectation at the time of making of the present invention of achieving a synergistic effect by combining the elements of the two cited references to reach the claimed invention herein, as suggested by the Examiner, as neither of the cited references recognizes the effect of tobacco smoke on ultraweak chemiluminescence of the skin. Thus, in view of the authorities cited above, it is believed that the instant rejection fails as a matter of law.

A method of measurement of environmental stress caused by contact of the skin to tobacco smoke by measurement of the increase in ultraweak chemiluminescence before and after exposure of the skin to tobacco smoke was unexpectedly discovered by Ms.

Egawa. Such unexpected discovery of the effects of tobacco smoke upon contact with the skin, the causes associated with the above mentioned environmental stress (which includes oxidation), and experimental data associated therewith, are discussed in the scientific paper entitled "Oxidative Effects of Cigarette Smoke On The Human Skin" previously filed herein, the authors of which include the present inventors Ms. Egawa and Mr. Kohno.

It was found that CL arises mainly from the decay of excited states generated during a chemical reaction, in this case oxidation caused by exposure of the skin to floating fine particles contained in tobacco smoke. The active species unexpectedly discovered by the present inventors to be related to CL include singlet oxygen, excited carbonyls and excited carbonic acid, which, upon exposure to free radicals contained in the tobacco smoke, become excited and chemiluminesce. This unexpected discovery (the prevention of free radicals contained in tobacco smoke from oxidizing the skin by applying the composition claimed herein) is in no way disclosed or suggested by the cited '806 reference, and constitutes an important element or aspect of the present invention.

In contrast, the '806 reference merely discloses that thiotaaurine destroys active oxygen *in vitro*. There is no disclosure whatsoever of the relation of ultraweak

chemiluminescence to oxidation of the skin, as was unexpectedly discovered by the present inventors and claimed herein.

Ultraweak chemiluminescence (CL) occurs on human skin, resulting from the radiation deactivation process of electrons from the excited state to the ground state. It was unexpectedly discovered that by monitoring the ultraweak chemiluminescence on human skin, it is possible to identify the oxidation reactions occurring on the skin (see Specification, page 20, paragraphs 2 and 3).

The inventors conducted tests, as described in "B-2. Testing of suppression of oxidation" (Specification, pages 24-26), wherein it was discovered that application of the claimed composition of the present invention to human skin could treat environmental stress effects on human skin by suppression of ultraweak chemiluminescence via suppression of oxidation of said skin.

In particular, as illustrated in Figure 3, it was unexpectedly discovered that the composition claimed herein reduces the ultraweak chemiluminescence on the skin, by reducing the level of oxidation reactions thereon (see Specification, page 26, 2nd paragraph), and that "reduction of the ultraweak chemiluminescence is particularly significant with glutathione and thiotaurine (see Specification, page 26, 3rd paragraph).

In view of the amendments made to the claims herein, the unexpectedness of the results obtained when implementing the method of the present invention, the deficiencies of the cited references, the lack of teaching or suggestion to combine same, and the legal authorities cited above, it is believed that the Examiner would be justified in no longer maintaining the present rejection. Withdrawal of the rejection is accordingly respectfully requested.

Reconsideration is respectfully requested of the rejection of claims 21-24, 26-28 and 29 under 35 U.S.C. §103(a) as being unpatentable over N'guyen et al. in view of Katsumata, et al. as applied to claims 1-4, 13-16, 20, 25 and 30-31 above, and further in view of Tominaga, et al. (5,747,049).

The N'Guyen, et al. and Katsumata, et al. references are discussed in detail above.

The secondary Tominaga '049 reference has an effective date of **May 5, 1998**, as no benefit of the filing date of the foreign application is given under 35 U.S.C. 102(e) for prior art purposes (see MPEP 706.02(f)(1)). In contrast, it is believed that the present application has a foreign priority date of March 30, 1997 via its' relation and claim to benefit of parent application serial No. 09/147,298. As required by 37 C.F.R. 1.55,

an English translation of said foreign priority document was filed in the parent application, and foreign priority benefits granted accordingly.

It is believed the presentation of said English translation, and the claim for benefit of foreign priority thereof, entitles the applicants to claim an effective filing date prior to the effective date of the cited reference. Thus, it is believed that the cited '049 reference is inapplicable as prior art in the instant application.

Regardless of the effective filing date accorded to the Tominaga reference, this secondary reference fails, as do the N'Guyen, et al. and Katsumata, et al. references, to recognize the link between environmental stress on causing an increase in ultraweak chemiluminescence of the skin caused by contact with tobacco smoke, the effect of the presently claimed composition in counteracting (suppressing) such increase in CL, and the method provided by the present inventors to do so. As the Examiner has correctly noted, Tominaga merely teaches the use of tannic acid, L-ascorbic acid phosphate and DL-alpha-tocopherol-L-ascorbic acid phosphate diester dipotassium, but fails to teach or suggest combining same with 0.001 to 5.0 wt% of sulfur containing amino acids selected from the group consisting of methionine, cystine, cysteine and glutathione, and 0.001 to 5.0 wt% of metabolic

intermediates of sulphur containing amino acids, said metabolic intermediates selected from the group consisting of homocysteine, sulfinic acid, cysteinic acid, thiocysteine, taurine, thiotaurine, hypotaurine, -djenkolic acid, cystathionine, S-allylcysteine, lanthionine and enthionine.

The method of application of a composition containing such a combination of elements to the skin, as claimed herein, was unexpectedly discovered by the present inventors to suppress ultraweak chemiluminescence of the skin caused by exposure of same with tobacco smoke. This teaching comes only from the present invention, and is neither taught nor suggested by the cited references, either alone or taken in combination.

In view of the above, it is believed that the combination of cited references fails to render claims 26-27 and 29 unpatentably obvious. As such, withdrawal of the rejection is accordingly respectfully requested.

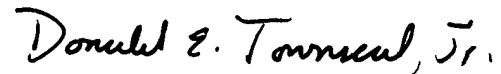
In view of the foregoing, it is respectfully submitted that the application is now in condition for allowance, and early action and allowance thereof is accordingly respectfully requested. In the event there is any reason why the application cannot be allowed at the present time, it is respectfully requested that the Examiner contact the undersigned at the number listed below to resolve any problems.

Respectfully submitted,

TOWNSEND & BANTA

A handwritten signature in cursive script, appearing to read "Donald E. Townsend".

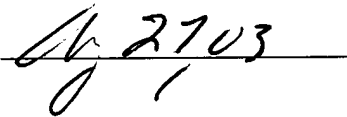
Donald E. Townsend
Reg. No. 22,069

A handwritten signature in cursive script, appearing to read "Donald E. Townsend, Jr.". The signature is written in a slightly more formal, upright cursive style.

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Date:

A handwritten date "8/27/03" written in cursive script, with a horizontal line drawn through the numbers.